

## Miscellaneous Pharmaco-active Substances and Nutritional Supplements: Education and Policy for Aircrewmembers

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### GENERAL DIETARY SUPPLEMENTAL ADVICE

Congress defined the term "dietary supplement" in the Dietary Supplement Health and Education Act (DSHEA) of 1994. A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandular extracts, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. They can also be in other forms, such as a bar, but if they are, information on their label must not represent the product as a conventional food or a sole item of a meal or diet. Whatever their form may be, DSHEA places dietary supplements in a special category under the general umbrella of "foods," not drugs, and requires that every supplement be labeled a dietary supplement. ***This Act, passed during the Clinton administration, shifted the burden to the FDA to prove that dietary supplements pose a significant or unreasonable risk rather than have the manufacturers bear the responsibility to establish the safety of the products they sell. A dangerous loophole considering many of the "supplements" have known pharmacoeactive properties and the fact the FDA often has few or inadequate data to evaluate, unless a group of investigators decides to independently conduct studies. Dr. Kessler from the Yale University School of Medicine has said, "Without a systematic review of safety and an adequate data base on safety, the American public remains at risk."***

#### Points to Remember:

- Harmful effects often associated with use in very high doses or in non-standard manner
- The U.S.P. notation indicated that a manufacturer has followed standards established by the US Pharmacopoeia and without it, one is essentially playing "Russian Roulette" with respect to bottle contents.
- Just because it might be "natural" doesn't mean it is safe
- Many may have beneficial effects in some users when used in moderation
- No method to test for most substances by urine or blood tests
- Flight Surgeons and other medical providers must be armed with "tools" to make informed decisions
- Aviators must be confident of accurate and informed counsel
- This list will require revision at least annually
- Must compel flight surgeons to discuss and document use of supplements at least annually. **\*\*Should be specific questions about nutritional supplements on SF/medical history form.**
- **Forms referring to "Medication" should be revised to read "medications or supplements"**
- Education
- Flight Surgeons, dietitians and healthcare providers engaged in care of special operational personnel should be offered educational blocks covering dietary supplements
- Possible venues include:
  - Flight Surgeon Primary Course
  - Entry level training
  - Continuing Education
- Studies may include performance enhancement qualities, specific aerospace effects (e.g. effects on G-tolerance), or literature base study of overall health effects
- As no current venue for aeromedical research into this area currently exists, cooperative study with civil and sister services may be considered
- FDA desires to have many recommendations regarding supplements by 2010.

#### Resources that may be helpful:

-U.S. Army Center for Health Promotion and Preventive Medicine  
<http://chppm-www.apgea.army.mil/dhpw>  
-The Center for Food Safety and Applied Nutrition  
<http://vm.cfsan.fda.gov>  
-Office of Dietary Supplements: <http://ods.od.nih.gov>  
-US Air Force <http://www.brooks.af.mil/af/altmed/HOMEFRAME.htm>

## **POLICY FOR SUPPLEMENTS AND VARIOUS PHARMACO-ACTIVE OTC ITEMS: CLASS A, B, and C**

### **CLASS A Substances for Class I, II, III (Use requires only documentation at annual physical)**

Substances For Which There is Strong Evidence of Safety and/or Efficacy. Limitations on quantity and type supplement shall be discussed **and documented** at time of annual physical according to the below.

#### **1. Sports drinks without creatine, ephedra, herbal supplements**

**Background:** Sport drinks not containing any of the compounds listed in Class B or Class C (i.e. ephedra, herbal compounds, glycerol, creatine) and contain only a mixture of carbohydrates, vitamins, and minerals, are allowed. These have been shown to help performance of continuous activity lasting longer than 90 minutes. However, they are not necessary if water is available. They are absorbed faster than water because of the added sugar and electrolytes and have added sodium, which stimulates thirst, stimulates drinking, and helps retain water.

Educating the aircrewmember about the type of safe and allowable sports drinks is essential. **Many sports drinks found at fitness centers and nutrition stores contain ephedra alkaloids (Class C) which have been strongly associated with adverse cardiovascular and central nervous system events** including: seizures, strokes, hypertension, arrhythmias, myocardial infarction, and death. Sports drinks containing caffeine are allowed, but should be strongly discouraged for their propensity to dehydrate and increase blood pressure and heart rate to potentially dangerous levels during exercise.

**Use in Aircrew: Sport drinks found in nutritional stores, gyms and other sources containing only carbohydrates, various mixtures of proteins, minerals/electrolytes and no compounds in Class B or C are allowed.**

#### **2. Protein Supplementation (form of shakes, capsules, nutrition bars)**

**Background:** A considerable amount of research has evaluated dietary protein needs of athletes. Although there is some debate, most studies indicate that in order to maintain protein balance during intense resistance and/or endurance training, athletes should ingest approximately 1.3 to 1.8 g protein per kg body mass per day. Athletes training at high-altitude may need as much as 2.2 g protein per kg per day in order to maintain protein balance. This protein intake is about 1.5 to 2 times the recommended dietary allowance (RDA) for the normal adult. In most instances an iso-energetic diet can provide the required protein, but athletes who maintain hypo-energetic diets, do not ingest enough quality protein in their diet, and/or train at altitude may be susceptible to protein malnutrition. In theory, this state could slow tissue growth and/or recovery from training.

**On the other hand, ingesting more protein than necessary to maintain protein balance during training (e.g., > 1.8 g/kg/d) does not promote greater gains in strength or fat-free mass.** These findings indicate that athletes typically do not need to supplement their normal diets with protein, provided they ingest enough quality protein to maintain protein balance. **Excessive amounts of protein intake can cause nausea, vomiting, and ultimately death in adults.**

**Use in Aircrew: Aircrew may supplement their diet with supplemental protein in the form of protein shakes, protein bars, or capsules, provided that the protein supplement does not contain supplements listed under Class C (creatine, ephedra, herbals, steroids) and the TOTAL amount of protein the aircrewmember consumes does not exceed 2 times the RDA value (1.58g/kg or .72 g/lb per day). Physicians must take into account the amount of protein coming from normal dietary sources (usually 12-15% of total calories comes from protein).**

### **3. Vitamins/Minerals**

**Background:** "Healthy adult men and healthy adult non-pregnant, non-lactating women consuming a usual, varied diet do not need vitamin supplements. Infants may need dietary supplements at given times, as may pregnant and lactating women. Occasionally, vitamin supplements may be useful for people with unusual lifestyles or modified diets, including certain weight reduction regimens and strict vegetarian diets." -*The American Medical Association*. Healthy children and adults should obtain adequate nutrient intakes from dietary sources. ***Meeting nutrient needs by choosing a variety of foods in moderation, rather than supplementation, reduces the potential risk of both nutrient deficiencies and nutrient excesses.*** Individual recommendations regarding supplements and diets should come from physicians and registered dietitians. Nutrients are potentially toxic when ingested in sufficiently large amounts. Safe intake levels vary widely from nutrient to nutrient and may vary with age and health of the individual. In addition, high dosage vitamin and mineral supplements can interfere with normal metabolism of other nutrients and with the therapeutic effects of certain drugs. The Recommended Daily Allowances represent the best currently available assessment of safe and adequate intakes, and serve as the basis for the U.S. Recommended Daily Allowances shown on many product labels. There are no demonstrated benefits of self supplementation beyond these allowances." *The American Institute of Nutrition, The American Society for Clinical Nutrition, The American Dietetic Association, and The National Council Against Health Fraud*. "A large percentage of people in the United States take dietary supplements, but not necessarily because of nutrient needs. The adverse effects of large doses of certain nutrients (e.g., vitamin A) are well documented. There are no documented reports that daily multiple vitamin-mineral supplements equaling no more than the RDA for a particular nutrient, are either beneficial or harmful for the general population. The potential risks or benefits of the long-term use of small doses of supplements have not been systematically examined." *Committee on Diet and Health, National Academy of Sciences, National Research Council*.

**NOTE: The best advice is to obtain vitamins and minerals by eating a wide variety of foods. If an individual chooses to take a multivitamin-multimineral supplement, a balanced diet also should be consumed. This is because knowledge is inadequate as to all of the essential nutrients needed by adults — all required nutrients may not be present in the supplement. Many multivitamin-multimineral supplements containing 100 percent U.S. RDA levels are on the market. The consumption of this level of supplement will not be harmful to health and may or may not be helpful. Taking high doses (1gram) of Vitamin C does not appear to prevent URI's in healthy subjects but may shorten the duration of the common cold to a small extent.**

**Use in Aircrew: Educate the aircrewmember. If a healthy adult wants to take a vitamin/mineral supplement, that supplement shall be a once-a-day multivitamin-multimineral from a USP labeled bottle.**

### **Tonic Water**

**Background:** Cinchonism is the well-known syndrome of quinine overdose involving disturbances of vision, hearing, and balance, which has occasional importance in aviation pathology, usually related to ingestion of tonic water. Ordinary social drinking of tonic water may lead to appreciable amounts of quinine in the body, although the levels are far lower than those commonly used in the treatment of malaria. The Armed Forces

Institute of Pathology (AFIP) in Washington, DC, found levels of 0.2mg/L in pilots in 3 fatal accidents in which positional cues seemed to be important. AFIP results show that commercial tonic water can contain 5.5-6.8 mg/dl. In the late eighties and early nineties, the Surgeon General of the Army medically restricted regular users of tonic water from flying and advised all aviators not to use it and Army aircrews were restricted from flying for 72 hours after ingestion of tonic water. It has been suggested that a chronic low-dose intake of quinine may accumulate in the endolymph of the human vestibular system and this accumulation could produce vestibular effects equivalent to a unilateral labyrinthectomy (see "The Bite of Jesuits' Bark", Aviation Space and Environmental Medicine, July, 1989).

**Use in Aircrew: Educate the aircrewmember about the risks associated with drinking tonic water regularly. Drinking more than three 12oz drinks per day (36 oz total) of tonic water is not authorized. Because tonic water is not classified as a supplement, it is important to ask at annual physical examinations if the aircrewmember drinks tonic water.**

### **CLASS B Supplements for Class I, II, III (Use Not prohibited but information required)**

Substances For Which Evidence Of Risk Is Minimal

•For all Class B supplements: Use requires consultation with flight surgeon and documentation of use in medical record. In addition, must have documented in medical record that specific guidelines of dosages, risks, benefits and side effects were discussed with aircrewmember. Supplements with the "USP" label are highly encouraged. Additional documentation needed is listed below for various supplements. Overall, the importance of educating the aircrewmember with some of the background information given below cannot be overstated.

#### **1. Glucosamine with or without chondroitin**

Background: Glucosamine (with or without chondroitin) may have some beneficial effect on osteoarthritis, and studies up to 3 yrs in duration have found no more adverse effects than with placebo, but most physicians are skeptical. Whether glucosamine offers any advantages over better-established drugs such as acetaminophen, traditional NSAIDs or selective COX-2 inhibitors remains to be determined. As with other dietary supplements, the quality and purity of the ingredients may vary (The Medical Letter, Vol. 43, Dec 20, 2001). American college of Rheumatology states it is too early to recommend its usage for osteoarthritis. NIH-sponsored randomized controlled trial ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) is currently in progress. Because of concerns regarding infectious contamination of chondroitin (a derivative of shark cartilage), glucosamine sulfate or glucosamine hydrochloride is recommended over glucosamine/chondroitin combinations.

**Use in Aircrew: Aircrewmember must be evaluated by the flight surgeon and diagnosis of osteoarthritis established. Educate the aircrewmember about the questions regarding the efficacy of these compounds vs. traditional anti-inflammatories and the lack of evidence demonstrating a structural modifying relationship. Dosage must not exceed 1500mg per day.**

**Grounding: 24 hour local grounding after first dose.**

**Waiver: Not required**

#### **2. Saw Palmetto (*Serenoa repens*)**

Background: A standardized liposterolic (fat-soluble) saw palmetto berry extract has demonstrated numerous pharmacological effects relating to its primary clinical application in the treatment of benign prostatic hyperplasia (BPH), a disorder caused by accumulation of testosterone in the prostate where a conversion to

dihydrotestosterone (DHT) takes place. The primary therapeutic action of saw palmetto extract in the treatment of BPH is thought to be a result of inhibition in the intraprostatic conversion of testosterone to DHT and inhibition of its intracellular binding and transport. However, more recent research has suggested other mechanisms including anti-estrogenic and receptor site-binding effects. In the United States, between 50 to 60% of men between the ages of 40 and 59 years have BPH. This disorder is characterized by increased urinary frequency, nighttime awakening to empty the bladder, and reduced force and caliber of urination. These major symptoms have been shown to be significantly improved in over dozen double blind, placebo-controlled clinical trials. In one of the larger studies involving 110 patients with BPH, impressive clinical results were reported: nocturia decreased by over 45%, flow rate (ml/s) increased by over 50%, and post-micturition residue (ml) decreased by 42% in the group receiving the serenoa extract. In contrast, those on placebo showed no significant improvement in nocturia or flow rate, and post-micturition residue actually worsened. Significant improvements were also noted in self-rating by the patients and global rating by the physicians. Of the 50 treated subjects completing the 30-day study, physicians rated 14 greatly improved, 31 improved, and only five unchanged or worsened. In contrast, no subjects in the placebo group had greatly improved, 16 showed some improvement, and 28 remained unchanged or worsened. No significant side-effects have been reported in the clinical trials of the saw palmetto berry extract or with saw palmetto berry ingestion. Long-term studies (3 years) have also failed to show any significant adverse effects other than gastric irritation.

***Use in Aircrew: Provided the aircrew member has been evaluated by the urologist who recommends the use of saw palmetto, the dosage for the liposterolic extract of saw palmetto berries (containing 85–95% fatty acids and sterols) is 160 mg twice daily. A similar dose using fluid extracts and tinctures is not authorized.***

**Grounding: 24 hours after first dose**

**Waiver: Not required.**

**CLASS C Supplements (Not authorized for use by any class)**

Dietary Supplements, Nutritional Supplements, and other preparations **containing** the following incapacitating /dangerous substances shall not be used by personnel in above categories. Many of these substances have either (1) proven to be hazardous or (2) have not been proven to be safe with no clear proven benefit

- Personnel taking these substances should be removed from aviation duty for a minimum of 24 hours after the last dose of the substance.

**Herbal Supplements:**

– <b>Aconitum napellus (wolfsbane)</b>
– Adonis vernalis (Pheasant’s eye)
– Atropa belladonna (Deadly Nightshade)*
– Cantharanthus roseum (Periwinkle)
– Chelidonium majus (Celandine)
– Conium maculatum (Hemlock)
– Convallaria majalis (Lilly of the Valley)
– Corynanthe yohimbe (Yohimbe bark)
– Cystisus scoparius (Broom)
– Datura stramonium (Jimson weed)*
– Datura stramonium (Thorn Apple)
– Digitalis lanata (Yellow foxglove)

– Digitalis purpurea (Purple Foxglove)
– Ephedra species (Ephedra)
– Exchscholzia californiica (California Poppy)
– GHB (Gamma Hydroxy Butyrate ) or GBL (Gamma-Butyrolactone) (may be known as Renewtrent, Revivarant, Blue Nitro, GH Revitalizer, Gamma G, Remforce)
– Humulus lupulus (Hops)
– Hyoscyamus niger (Henbane)*
– Hypericum Perforatum (St. Johns Wort)
– Lactuca virosa (Wild lettuce)
– Lycopodium serratum (Jin Bu Huan)
– Mandragora officinarum (Mandrake)
– Myristica fragrans (Nutmeg)in large quantities
– Papaver somniferum (Opium poppy)
– Passiflora incarnata (Passion flower)
– Piper methysticum (Kava-Kava)
– Psilocybe semilanceata (magic mushrooms)
– Rauwolfia serpentina (Indian snakeroot)
– Rauwolfia serpentina (Indian Snakeroot)
– Scilla maritima (White Squill)
– Scopolia carniolica (Scopolia)*
– Scutellaria laterfoloia (Skullcap)
– Strophanthus kombe (Strophanthus)
– Urginea maritima (Squill)
– Valeriana officinalis (Valerian)

Dietary Supplements, Nutritional Supplements, and other preparations **containing** the following *potentially* harmful substances shall not be used by personnel in above categories.

- Personnel taking these substances should be removed from aviation duty for a minimum of 24 hours after the last dose of the substance.

#### **Anabolic Steroids:**

– <b>*Zeranol</b>
– *Testosterone (Malogen, Malogex, Delatestryl)
– *Stanozolol (Winstrol, Stromba)
– *Oxymetholone (Anadrol, Anapolon 50, Adroyd)
– *Oxandrolone (Anavar)
– *Norethandrolone (Nilevar)
– *Nandrolone (Durabolin, Deca-Durabolin, Kabolin, Nandrobolic)
– *Methyltestosterone (Android, Estratest, Metandren, Virilon, Oreton Methyl, Testred)
– *Methandrostenolone (Dianabol)
– *Metenolone (Primobolan, Primonabol-Depot)
– *Metandienone (Danabol, Dianabol)
– *Mesterolone (Androviron, Proviron)
– *Human Chorionic Gonadotrophin

– *Growth Hormone
– *Fluoxymesterone (Android F, Halotestin, Ora-Testryl and Ultradren)
– *Dihydrotestosterone (Stanolone)
– *DHEA
– *Dehydrochloromethyl Testosterone (Turinabol)
– *Danocrine
– *Danazol
– *Clostebol (Steranobol)
– *Clenbuterol
– *Boldenone (Equipoise)
– *Bolasterone (Vebonol)
– *Androstendione (Androsten and others)

**Glandular Extracts:**

– <b>Teucrium spp. (Germander)</b>
– Testicular extracts
– Symphytum officinale (Comfrey)
– Senecio spp (thread leafed groundsel and Life root)
– Larria tridentata (chaparral)
– Aortic extracts
– Adrenal Extract

**Other Compounds:**

– <b>Pangamic Acid (Vitmain B15)</b>
- Echinacea species
- Creatine
- Amino Acid Supplements (Anabolic and Branched Chain), Beta-Hydroxy-Beta Methylbutyrate (HMB)
- Coenzyme Q (CoQ10), Choline, L-Carnitine, Chromium Picolinate, Phosphate salts, vanadyl sulfate
- Glycerol
– Any supplement not listed in this policy in considered Class C, until further research indicates otherwise

**Background on Class C Supplements**

**Plant Products (Herbs)**

– *Psychiatric effects*

— **Sedation**

– Some substances used in “medicinal” doses (exceeding sprinkled on spices) are known to have sedative properties.

- Their effects may be additive with other over the counter or prescription agents with sedative properties.
- The duration of action is unpredictable
- Research into their effects on specific areas of concentration and tracking tasks is lacking.
- **Plant products known or likely to be sedatives:**
  - *Valeriana officinalis* (Valerian)
  - *Rauwolfia serpentina* (Indian snakeroot)
  - *Atropa belladonna* (Deadly Nightshade)\*
  - *Chelidonium majus* (Celandine)
  - *Humulus lupulus* (Hops)
  - *Conium maculatum* (Hemlock)
  - *Lycopodium serratum* (Jin Bu Huan)
  - *Papaver somniferum* (Opium poppy)
  - *Passiflora incarnata* (Passion flower)
  - *Scutellaria laterifolia* (Skullcap)
  - *Lactuca virosa* (Wild lettuce)
  - *Aconitum napellus* (wolfsbane)
  - *Hyoscyamus niger* (Henbane)\*
  - *Datura stramonium* (Jimson weed)\*
  - *Scopolia carniolica* (Scopolia)\*
    - \*anticholinergic actions
- **Synthetic Agents known or likely to be sedatives**
  - GHB (Gamma Hydroxy Butyrate)
    - Renewtinent, Revivarant, Blue Nitro, GH Revitalizer, Gamma G, Remforce
  - Is a CNS depressant associated with several deaths especially if used with ETOH
    - Pure form experimentally used for some sleep disturbances (controlled drug)
  - Marketed as agent to enhance fitness, reduce stress and enhance sex drive
    - Precursor agents (GBL) marketed openly (although illegally in most states)
  - FDA has issued do not use warnings.
- **Hallucinations**
  - Some plants, sometimes smoked to release high concentrations of volatile oils, are capable of causing hallucinations or altered sensorium
  - These are not widely marketed by mainstream companies, but are often available through other sources
  - **Plant products known or suspected to cause hallucinations or altered sensorium:**
    - *Psilocybe semilanceata* (magic mushrooms)
    - *Exchscholzia californiica* (California Poppy)
    - *Piper methysticum* (Kava-Kava)
    - *Mandragora officinarum* (Mandrake)
    - *Myristica fragrans* (Nutmeg)in large quantities
    - *Cantharanthus roseum* (Periwinkle)
    - *Datura stramonium* (Thorn Apple)
    - *Corynanthe yohimbe* (Yohimbe bark)
- **Cardiovascular effects**
  - **Cardiac glycosides**
  - Cardiac glycosides may precipitate dysrhythmias; especially when found in association with electrolyte abnormalities such as would occur with poor hydration status (digitalis family).
  - **Plant products known to contain cardiac glycosides or cardioactive substances**
    - *Digitalis purpurea* (Purple Foxglove)
    - *Urginea maritima* (Squill)
    - *Cystisus scoparius* (Broom)
    - *Convallaria majalis* (Lilly of the Valley)
    - *Adonis vernalis* (Pheasant's eye)
    - *Strophanthus kombe* (Strophanthus)

- *Scilla maritima* (White Squill)
- *Digitalis lanata* (Yellow foxglove)
- **Vasoactive substances**
  - **Stimulant (s)**
  - Contain powerful sympathomimetic agents that directly stimulate the heart and blood vessels.
  - Have been implicated in deaths due to stroke or heart attack attributed to massive increases in pulse and blood pressure, and have been responsible for mission failure due to palpitations.
  - **Substances known to be potent cardiovascular stimulants**
    - *Ephedra species* (*Ephedra*)
  - **Hypotensive Agent(s)**
  - These plants elaborate substances that relax blood vessels lowering blood pressure.
    - Such products would potentially affect Gz tolerance
  - Plant products known to contain substances with cardiovascular activity:
    - *Rauwolfia serpentina* (*Indian Snakeroot*)
- **Specific Therapies Felt To Pose A Risk to Overall Health:**
- **Liver Toxins**
  - **Pyrollizidine Alkaloids**
    - A number of plants elaborate pyrollizidine alkaloids, known to cause harm to the liver
    - Such damage is often irreversible, and may result in permanent disability or death.
    - Reaction to these alkaloids is poorly understood, and may not be totally dependent on dose
    - **Substances known or believed to be toxic to the liver**
      - *Senecio spp* (*thread leafed groundsel and Life root*)
      - *Larria tridentata* (*chaparral*)
      - *Symphytum officinale* (*Comfrey*)
      - *Teucrium spp.* (*Germander*)
- **Anabolic Steroids-**
  - Many synthetic agents are currently available as dietary supplements. Most are steroids marketed for body builders. Adverse effects of anabolic steroid use include behavioral changes, testicular atrophy and reduced sperm production, gynecomastia, and baldness.
  - Long-term effects include increased atherogenesis; increased risk of stroke or heart attack due to increased platelet aggregation, and direct damage to the heart and liver
- **Glandular Extracts**
  - **Background:** A wide variety of animal tissues have been processed to provide various health effects primarily related to their retained hormone effects.
    - Content of these extracts may be lost during digestion
    - Some appear to retain their biological activity although to what degree is unpredictable
    - All carry with them some risk of infectious transmission (especially prions and viruses)
  - **Commonly used glandular extracts include**
    - *Adrenal Extracts*
    - *Testicular extracts*
    - *Aortic extracts*
- **Other Compounds (Pangamic Acid or Vitamin B15)**

**Background:** Although claiming to be a vitamin, this is not a true vitamin and is a mixture of a calcium compound and gluconate. It may contain a variety of compounds. There is no evidence to support the claim that it improves endurance and several of the compounds marketed under this name are potentially hazardous.
- **Echinacea products**

Background: Several well-documented reports of allergic skin reactions and anaphylaxis are associated with these plant products. There is no convincing evidence that echinacea decreases the severity or shortens the duration of upper respiratory infections and the purity and potency is highly variable as with other dietary supplements. In the studies where a significant effect was seen, there are several concerns methodologically speaking on how the studies were conducted.

#### - **Creatine**

Background: Although creatine came onto the scene as a performance promoter for the physically active individual, there are **several questions about performance gains and safety that preclude it being authorized for general use in aircrew at this time.** The benefits of supplementation on performance are limited to specific types of activities. Preliminary information suggests that high-intensity, short duration activities may benefit from creatine supplementation. Some examples include weight training, baseball, sprinting, throwing, jumping, football, and soccer. However, only people with low levels of muscle creatine will benefit from creatine supplementation. Testimonial reports imply that creatine supplementation can cause nausea, vomiting, diarrhea, kidney and liver problems, high blood pressure, and muscle cramps/strains/pulls and no safety for long-term use has been shown. As a testimony to its medicinal properties, creatine supplementation has been carefully prescribed in the medical community and used with success in various mitochondrial and neuromuscular disorders to increase muscle function and strength.

France actually forbids the sale of any products containing creatine and Italy allows its use but only under the strict supervision of a physician and only for certain pathological conditions. Furthermore, because of poor manufacturing processes and lack of stringent quality control here in the US, various contaminants present in creatine products (such as dicyandiamide, creatinine, etc.) may pose a health risk and also precludes recommendation at this time. **Creatine should always be avoided by those who seek to lose weight while exercising heavily in hot and humid conditions.** Preliminary findings indicate that creatine supplements may selectively reduce plasma volume, which impairs the capacity to sweat and thus decrease the ability to maintain a normal body temperature during exercise in hot, steamy conditions. **In contrast to high-intensity or anaerobic activities, creatine supplementation does not improve, and may even worsen, endurance performance.** One study found that marathon runners had poorer performances after creatine loading. There is one consistent side effect of creatine supplementation - a small weight gain, most likely from water accumulation and the effect of this in the aviation environment has not been studied. Future studies need to address some practical issues. These issues include development of safe and effective programs to maximize muscle creatine accumulation and to maintain elevated creatine stores, determination of long term side effects of creatine supplementation, and assessment of its effects in women and the elderly. In time, as more studies focus on long term safety issues and quality issues are addressed by the FDA, a safe recommendation on use and dosages might be possible. As mentioned above, the one promising area at this time is the use of creatine supplementation to restore muscle function in patients with muscle loss and specific types of nerve and muscle diseases. Creatine "loading" (20-30 grams/day) has been a common practice among a variety of athletes. More recent research indicates, however, that much smaller doses of creatine (3 to 5 grams daily or 1 pound of beef) in excess of the usual intake of 2 grams are equally effective in elevating muscle creatine and phosphocreatine.

#### - **Amino Acid Supplements (Anabolic and Branched Chain), Beta-Hydroxy-Beta Methylbutyrate (HMB)**

Background: There is some evidence from clinical populations that certain amino acids (e.g., arginine, histidine, lysine, methionine, ornithine, and phenylalanine) may stimulate the release of growth hormone, insulin, and/or glucocorticoids and thereby promote anabolic processes. However, there is little evidence that supplementation of these amino acids provides ergogenic benefit for athletes. Branched-chain amino acids and glutamine have been hypothesized to affect central fatigue and exercise-induced immune suppression, but their ergogenic value during prolonged exercise is equivocal at present. Furthermore, published studies of safety have not fully taken account of chronic consumption by healthy subjects of all age groups. Side effects seen with intake of individual amino acids were mostly neurological in nature.

Because glutamine is metabolized to glutamate and ammonia, both of which have neurological effects, psychological and behavioral testing may be appropriate if adverse effects are suspected in any patient. Human studies are inconclusive about the effectiveness of HMB, a breakdown of leucine, and more research is needed.

- **Coenzyme Q (CoQ10), Choline, L-Carnitine, Chromium Picolinate, Phosphate salts, vanadyl sulfate**

Background: Carnitine is involved in the metabolism of fats and is prevalent in a variety of animal products. It is claimed to increase aerobic power and energy level as well as decrease body fat. Some performance benefit is seen with repeated, very intense exercise, but there is no evidence it decreases body fat. The body generally makes adequate amounts. Choline is a constituent of cell membranes and is promoted to decrease body fat, delay fatigue and promote faster recovery. There is NO evidence it improves performance or reduces body fat. Supplements may cause diarrhea, foul smelling intestinal gas, and may cause a “fishy” body odor. Found in egg yolks and meats and deficiencies are very uncommon. Coenzyme Q, or CoQ10, is an enzyme component found in mitochondria of cells. It is a potent antioxidant and is claimed to increase energy and cardiac performance. NO benefits have been reported in athletes. It has been used with therapeutic success in patients with heart disease to increase oxygen utilization and exercise performance and has also been shown to increase submaximal and maximal exercise capacities in sedentary men. With regards to chromium picolinate, phosphate salts, and vanadyl sulfate, research is either ambiguous or inadequate to support performance enhancement. Long term safety cannot be assumed or expected. Because of this, and the lack of proven benefits, they are not authorized at this time.

- **Glycerol**

Background: Some studies have shown glycerol to be an effective ergogenic aid, most of these have methodological problems. Data and reviews from USARIEM (US Army Research Institute of Environmental Medicine) do not support the use of glycerol as an ergogenic aid (see Latzka and Sawka, Can J Appl Physiol, 25 (6): 536-545, 2000). More importantly, the clinical use of oral glycerol in reducing intraocular pressure and other medical anomalies (0.25-2g/kg) is effective because, although acute glycerol administration results in increased total body water (hyperhydration), it then turns into a potent osmotic dehydrating agent. This can be potentially dangerous in the post-exertion period as diuresis coupled with exercise dehydration could produce volume/ electrolyte abnormalities. Also, at doses around 1g/kg, many people experience nausea/vomiting from glycerol.

**CFSAN****CENTER FOR FOOD SAFETY & APPLIED NUTRITION**

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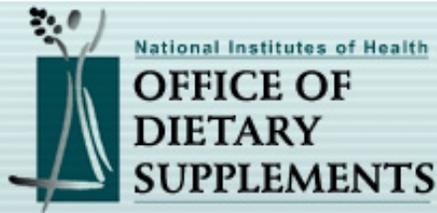
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Office of Dietary Supplements

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## Virtual Flight Surgeon (Civilian Link)

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